920-33 Neutrophil Activation in Unstable Coronary Artery Disease

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Neutrophil (PMN) activation and aggregation appear to be important inflammatory events of the atherosclerotic process. To determine whether PMN activation occurs by proximity to "unstable" atherosclerotic plaques, we studied PMNs that traverse the coronary circulation of patients with unstable angina (UA; 63.1 ± 2.2 years).

Blood samples were collected simultaneously from the aorta and coronary sinus (CS) during coronary arteriography in patients with UA, with stable angina (SA; 60.1 ± 1.9 years) and with angiographically normal coronary arteries (58.1 ± 2.1 years). All patients were on aspirin. PMNs were separated and the generation of superoxide (reduction of cytochrome *c* technique, nmol $\cdot O_2^-/10^6$ cells) and aggregation (amplitude, cm/min) of *ex vivo* phorbol myristate acetate (100 ng/ml)-stimulated PMNs were measured.

Results:

Group	Superoxide		Aggregation	
	Aorta	CS	Aorta	CS
UA (N = 12)	4.2 ± 0.9	1.7 ± 0.9*	3.5 ± 0.4	1.2 ± 0.4*
SA (N = 12)	3.9 ± 1.9	8.7 ± 2.8*	3.9 ± 0.8	7.6 ± 0.6*
Normal (N = 11)	4.0 ± 1.0	7.7 ± 2.2*	2.1 ± 0.8	7.3 ± 1.1†

Data expressed as Mean ± SEM. CS *vs* aorta: P ≤ *0.05, †0.02.

Superoxide generation and aggregation decreased significantly in stimulated PMNs of UA patients suggesting *in vivo* activation. These data indicate that "unstable" atherosclerotic plaques induce PMN activation and hyperaggregability and suggest a potential role of an inflammatory process in the progression of atherosclerosis.

920-34 Different Contractile Effects of Ergonovine and Methylergonovine in Isolated Human Coronary Arteries

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Ergonovine maleate (E) and methylergonovine maleate (M) have been equivalently used to provoke coronary vasospasm in patients with variant angina. Large epidemiological studies with these drugs revealed varying incidences of positive results in different patient populations. Head to head comparisons of the test sensitivities and the dose dependencies of their effects are not available. In the present study we directly compared the contractile effects of E and M in isolated human coronary arteries in the presence or absence of the thromboxane analogue U 46619 (U46), since thromboxane potentiates serotonin-induced contractions in human coronary arteries. The arteries were obtained from explanted hearts of patients with dilated cardiomyopathy during heart transplantation. Changes in isometric force were recorded in rings with intact endothelium mounted in organ chambers. The rings were exposed to increasing concentrations of E or M (10^{-9} to 10^{-5} M) in the presence or absence of U46 (10^{-9} M), which itself does not significantly affect coronary tone.

Results:

	M	E	M + U46	E + U46
10^{-7} M	7 ± 3	6 ± 2	4 ± 3	33 ± 6*
10^{-6} M	8 ± 2	9 ± 2	3 ± 1	38 ± 8*
10^{-5} M	10 ± 3	12 ± 4	−3 ± 6	39 ± 10*

change in tension in % of contraction to potassium chloride 60 mM, means ± SEM of 6 experiments in each group; *p < 0.05.

Thus E and M are weak vasoconstrictors in quiescent human coronary arteries with comparable potency. However, the drugs differ regarding the potentiation of their effects by thromboxane. Provocation with M may not reveal coronary vasospasm due to thromboxane-induced supersensitivity to serotonin.

920-35 Matrix Metalloproteinase Activity in Morphologically Stable and Vulnerable Atherosclerotic Plaques

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Atherosclerotic (AS) plaques that undergo rupturing and thrombosis contain large amounts of lipids and numerous macrophages. We investigated the presence and activity of extracellular matrix degrading enzymes in human AS plaques in relation to the presence of macrophages.

Thirteen AS plaques and 5 normal vessel walls from human coronary arteries and aortas were obtained at autopsy. Cryostat sections were cut for immunocytochemistry to study cell composition of the plaques using a smooth muscle cell (SMC) anti-actin/macrophage (anti-CD68) double stain and the expression of matrix metalloproteinases (MMPs) using anti-MMP 2 and 9 (gelatinases) and anti-MMP 3 (stromelysin) antibodies. The remaining frozen plaque tissue was homogenized and used for gelatin zymography to establish MMP 2 and 9 activity per mg plaque tissue.

Three plaques showed ruptures and contained numerous macrophages but a low number of SMCs. Of the 10 uncomplicated plaques, 7 were macrophage-rich and 3 were fibrous/SMC-rich. All MMPs were immunolocalized in the plaques studied, the amount being increased in macrophage-rich areas, especially around lipid cores. This was consistent with the biochemical results: high amounts of both zymogen and active forms of MMP 9 (92 and 88 kD, respectively) and MMP 2 (72 and 68 kD, respectively), but much lower activity of these enzymes in fibrous lesions and normal arteries.

The finding of abundant gelatinase activity and stromelysin expression in lipid/macrophage-rich intact plaques (prone to rupture) and in ruptured plaques but lower in fibrous plaques (stable lesions) strongly suggest involvement of tissue degrading enzymes in the process of plaque weakening prior to rupture.

920-36 Release of Troponin I From Short-Term Hibernating Myocardium Subtending Severe Coronary Stenosis

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Loss of myofilaments has been observed in short-term hibernating myocardium with contractile dysfunction subtending a severe coronary stenosis with reduction of resting coronary flow. Troponin I (T) is an important myocardial protein to regulate the contractile process. To examine whether short-term hibernating myocardium is associated with loss of the regulatory protein T, we created an LAD stenosis in 8 pigs to reduce resting coronary flow by 40%; the stenosis was maintained for 24 hours to 7 days. Coronary flow was measured by a flowmeter and regional wall thickening monitored by echocardiography. Blood samples for T were drawn at baseline, 6 hours (h), 24 h and then daily for 7 days. T was determined by fluorogenic ELISA assays. Hearts were sectioned for gross and microscopic inspection for infarction.

Results: No infarction was noted in 5 pigs and the other 3 had patchy necrosis involving less than 4% of area at risk. Echocardiography documented persistent regional LV dysfunction. T increased during the development of myocardial hibernation, peaking at 24 hours and returning to normal within 5–6 days (see Table). T increased in pigs with and without patchy necrosis:

	Baseline	Stenosis	6 h	24 h	3 days	6 days
T (ng/ml)	0.2 ± 0.3	20 ± 13	66 ± 70	110 ± 50	30 ± 11	0.8 ± 0.7

Conclusions: In this model of a severe coronary stenosis that reduces coronary flow and induces regional dysfunction, troponin I is released and may be related to the loss of myofilaments in hibernating myocardium.

921 New Stents

Monday, March 25, 1996, 3:00 p.m.–5:00 p.m.
Orange County Convention Center, Hall E
Presentation Hour: 3:00 p.m.–4:00 p.m.

921-37 Favorable Arterial Remodeling and Reduced Neointimal Formation With a Nitinol Self-Expanding Stent

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Intracoronary stent placement with the Palmaz-Schatz stent is associated with a lower incidence of restenosis as compared to PTCA. The physical properties of a stent designed to further reduce restenosis have not been determined. We compared the coronary arterial response to a novel nitinol self-expanding stent with the Palmaz-Schatz stent. Twelve stents (6 nitinol and 6 Palmaz-Schatz) were implanted in the coronary arteries of six swine. The nitinol stents were deployed using the intrinsic thermal properties of